26th Annual Infectious Diseases Research Day

&

13th Annual Canadian Center for Vaccinology Symposium

DALHOUSIE UNIVERSITY
FACULTY OF MEDICINE
Continuing Professional Development

Canadian Center for Vaccinology
Dalhousie University
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April 20, 2021
Halifax, Nova Scotia

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In keeping with CMA Guidelines, program content and selection of speakers are the responsibility of the planning committee. Support is directed toward the costs of the course and not to individual speakers through an unrestricted educational grant.

Thank you!

This program is supported in part by contributions provided by:

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Yayha Shabi
Zhenyu Cheng

Welcome to the 26th Annual Infectious Diseases Research Day and 13th Annual CCfV Symposium!

Karina Top, MD, MS, FRCPC
Division of Infectious Diseases, Departments of Pediatrics and Community Health & Epidemiology

Welcome to the 2021 Infectious Diseases Research Day and CCfV Symposium. This annual event provides a unique learning opportunity for researchers, trainees, public health professionals, healthcare providers, and community members featuring experienced presenters, and inspired research trainees. Our goal is to highlight Canadian research by established investigators, as well as showcase emerging talent. Our program this year is filled with a variety of presentations and posters on various aspects of vaccinology and COVID-19, from basic science to policy and programs. We aim to identify research strengths and build new collaborations to extend local research connections.

Welcome and thank you for joining us!

Scott Halperin MD, FRCPC
Director
Canadian Center for Vaccinology

The Infectious Diseases Research Day and CCfV Symposium offers a fascinating platform that allows local researchers to present their work and learn about the work of their colleagues. We encourage you all to take part in this one-day event that will feature interesting topics surrounding infectious diseases.

I would like to offer my sincerest thanks to our planning committee and the financial support from our corporate sponsors. This event would not be possible without the dedicated work and continued support from these individuals.

26th Annual Infectious Diseases Research Day & 13th Annual Canadian Center for Vaccinology Symposium

Schedule of Events

Tuesday, April 20, 2021

8:00am – 4:30pm

*All presentations will be done online through Microsoft Teams & Zoom

Posters submitted for viewing can be reviewed all day at the following link:
http://centerforvaccinology.ca/2021posters/

8:00 – 9:00am TJ Marrie Lecture
Join Zoom Meeting
Presenter: Dr. Karen Doucette, *Increased Infection Risk Organ Donors (IRD): The Importance of Language in Medicine*

9:20 – 9:30am Welcome and opening remarks - Dr. Scott Halperin and Dr. Karina Top
Click here to join the meeting

9:30am – 12:35pm Oral Presentations

9:30am	Brett Duguay
9:47am	Duncan MacKenzie
10:04am	Stacia Dolliver
10:21am	Farhan Khan
10:38am	Lauren MacDonald
10:55am	BREAK
11:12am	Michal Scur
11:29am	Brendon Parsons
11:46am	Terra Manca
12:03pm	Siena Davis
12:20pm	Monica Surette

12:35 – 1:00pm Break

1:00 – 2:00pm Poster Presentations (concurrent sessions)

	Group 1 Click here to join the meeting		**Group 2** Click here to join the meeting
	PhD/Post Docs:		Residents/Research Staff:
1:00pm	Animamalar Mayavannan	**1:00pm**	Sharon Oldford 1

1:06pm	Gayani Gamage	**1:06pm**	Sharon Oldford 2
1:12pm	Patrick Slaine	**1:12pm**	Carrie Phillips
		1:18pm	Erin Ring
	Faculty:	**1:24pm**	Yahya Shabi
1:18pm	Melissa Andrew and Shelly McNeil	**1:30pm**	Shawn Smith
1:24pm	Melissa Andrew		
			Faculty:
	Masters:	**1:36pm**	Emily Black
1:30pm	Taylor Caddell	**1:42pm**	Sam Meeker
1:36pm	Daniel Medina-Luna (PhD)	**1:48pm**	Voica Racovitan 1
1:42pm	Madeleine Stolz	**1:54pm**	Voica Racovitan 2
	Faculty:		
1:48pm	Emma Reid		
1:54pm	Kaela Fraser		

Click here to join the meeting

2:00 – 3:00pm Presentation
Presenter: Dr. Brian Ward, *Venture Capital and Vaccines: Repurposing an Attenuated Salmonella as an Oral Vector for a C. difficile Vaccine*

3:00 – 3:15pm Break

3:15 – 3:45pm Presentation
Presenter: Dr. Joanne Langley, *Canada's COVID-19 Vaccine Response One Year In*

3:45 – 4:15pm Presentation
Presenter: Dr. Lam Ho, *Statistical Analysis for Emerging Infectious Diseases*

4:15 – 4:30pm Awards ceremony

Educationally co-sponsored by Dalhousie University Continuing Professional Development

This program is supported by educational grants from

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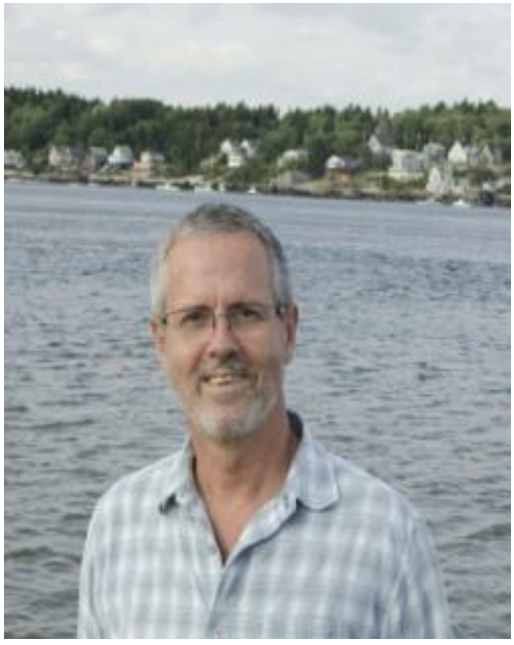
Speakers

Dr. Karen Doucette

Dr. Doucette completed her undergraduate (BSc) degree and MD at Dalhousie University in Halifax, Nova Scotia. Internal Medicine training at Queen's University was followed by subspecialty training in Infectious Diseases at the University of Manitoba. While at University of Manitoba she undertook additional subspecialty training in viral hepatitis and liver disease. In 2003 she completed a clinical and research fellowship in Transplant Infectious Diseases under the supervision of Dr. Jay Fishman at the Massachusetts General Hospital. In 2007 she completed a Master's in Epidemiology at Harvard School of Public Health. She was appointed Assistant Professor at the University of Alberta in 2004, promoted to Associate Professor in 2010 and to full Professor in 2018. In 2015, she was appointed Divisional Director and Edmonton Zone Section Chief of Infectious Diseases.

Her clinical and research interests are in infections in immunocompromised hosts, particularly solid organ transplant recipients, and viral hepatitis. She was the Medical Director for the Infectious Diseases Hepatitis Support Program from 2006-April 2015 and led the Transplant Infectious Diseases Program from 2004 to 2008. She has published over 50 peer reviewed manuscripts as well as authored or co-authored several book chapters and both national and international guidelines in the fields of transplantation and viral hepatitis. As acknowledgement of her expertise in these fields, she has delivered eight international and over 30 national scientific lectures. As well as over 200 CME sessions regionally and nationally. In 2016 she was inducted in the second cohort of Fellows of the American Society of Transplantation.



Dr. Brian Ward

Dr. Ward was trained at McGill, Oxford, University of London and Johns Hopkins. He returned to McGill in 1991 where he is currently a professor in Infectious Diseases and Tropical Medicine. Dr. Ward has served in many different roles nationally and internationally in matters related to global health and vaccines. He has received a number of honors and awards including a Rhodes scholarship (1977), the US Exceptional Public Service Award (2003) and he was elected to the Canadian Academy of Health Sciences in 2012. Among other responsibilities, he currently chairs of the Scientific Advisory Board for the CIHR Institute of Infection and Immunity. Since 2010, he has served as medical officer for Medicago Inc. He has a range of research interests and has published >270 peer-reviewed manuscripts.

Speakers

Dr. Joanne Langley

Dr. Joanne Langley is a Professor of Pediatrics and Community Health and Epidemiology at Dalhousie University and the Canadian Center for Vaccinology in Halifax, NS Canada, head of Pediatric Infectious Diseases at the IWK Health Centre, and lead for the Clinical Trials Network of the Canadian Immunization Research Network. She currently co-chairs the Canadian COVID-19 Vaccine Task Force. Her research is focused on the epidemiology and vaccine prevention of respiratory infections, particularly Respiratory Syncytial Virus and influenza, and immunization decision making.

Dr. Lam Ho

Dr. Lam Ho is currently an Assistant Professor and a Canada Research Chair (Tier 2) in Stochastic Modelling at the Department of Mathematics and Statistics, Dalhousie University. He received his Ph.D. in Statistics from the University of Wisconsin-Madison in 2014. Before joining Dal, he worked as a postdoctoral researcher at the University of California, Los Angeles. Dr. Ho is interested in statistical theory and methods for stochastic models in evolutionary biology and infectious disease epidemiology.

Oral Presentations

(Presenter's name in **bold)**

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Oral Presentation Abstracts

(Presenter's name in **bold)**

Oral Presentation 1

Title: THIOPURINES STIMULATE THE UNFOLDED PROTEIN RESPONSE RESTRICTING HUMAN CORONAVIRUS REPLICATION

Authors: BA Duguay, ES Pringle, E Kadijk, S Ying, P Slaine, DA Khaperskyy, C. McCormick

Affiliation: Dalhousie University

Introduction: The need for effective and accessible antivirals has remained largely unmet. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) pandemic is a stark reminder of the inadequacy of our tools to combat viral diseases. Developing novel antivirals and repurposing existing medications are valuable strategies to develop new treatments. Host-directed antivirals (HDAs) are a class of antivirals that modulate host functions and render the cellular environment less permissible to infection. We identified 6-thioguanine (6-TG, Lanvis®/Tabloid®) and its derivative 6-thioguanosine (6-TGo) as effective HDAs against human alpha- and beta-coronaviruses.

Methods: We employed cell culture models of human coronavirus (HCoV) infection in HCT-8/BHK-21 cells (OC43) and Huh7.5 cells (229E) to examine virus production following treatment of cells with thiopurines 6-TG, 6-TGo, 6-mercaptopurine (6-MP, Purinethol®), or an unfolded protein response (UPR) agonist, tunicamycin (Tm). Differences in viral protein production, UPR induction, or genome copy number were analyzed by western blotting and qRT-PCR. The effects of 6-TG and the UPR on SARS-CoV-2 Spike (S) protein production was examined in transfected HEK293 cells.

Results: Treatment with 6-TG or 6-TGo reduced viral titres of HCoV-OC43 and HCoV-229E by 30 to 40-fold at 24 h post-infection. These observations correlated with reductions in viral genomes in infected cells as well as reductions in viral protein during infection (HCoV-OC43 nucleoprotein) or overexpression (SARS-CoV2 S) experiments. 6-TG and 6-TGo were observed to induce UPR signaling (upregulation of CHOP or BiP expression) in uninfected and infected cells. This resulted in the upregulation of endoplasmic reticulum (ER)-associated protein degradation (ERAD)-mediated decay of the SARS-CoV2 S glycoprotein in transfected cells. The related thiopurine, 6-MP, had minimal effects on viral titres or viral protein expression.

Conclusions: 6-TG and 6-TGo are effective inhibitors of HCoV replication in cell culture. These drugs establish an antiviral environment by inducing the UPR, which in turn negatively effects the production and accumulation of viral proteins. These data highlight the utility of targeting the UPR as a practical antiviral strategy.

Oral Presentation 2

Title: SERUM FROM CONVALESCENT SARS-COV-2 PATIENTS CAN INHIBIT SPIKE-DEPENDENT CELL-TO-CELL FUSION

Authors: D MacKenzie*[1], Greenshields, A.L.*[2], Pringle, E.S.*[1], McMullen, N.[1], Charman, M.[1], McCormick, C.[1], Liwski, R.[2], Duncan, R.[1]

Affiliation: [1]Department of Microbiology & Immunology, Dalhousie University, [2]Department of Pathology, Dalhousie University; *Equal contribution.

Introduction: Approved vaccines for SARS-CoV-2 target the viral Spike glycoprotein. Spike binds the ACE2 receptor protein and mediates fusion of viral and host cell membranes to complete the entry process. Antibodies that bind Spike and prevent association with ACE2 are sufficient to neutralize infectious virus and appear sufficient to prevent severe disease in vaccinees. Spike is also expressed on the surface of infected cells and can drive cell-to-cell fusion with ACE2-expressing cells. Cell-to-cell fusion increases membrane permeability and stimulates pro-inflammatory cell death, which might contribute to disease severity in COVID-19. It remains unclear if antibody responses that neutralize virus infection can similarly neutralize cell-to-cell fusion and if different antibody isotypes are required for these functions.

Methods: 72 human convalescent sera (HSC) were purchased from BioIVT and Access Biologicals. This panel and several controls were evaluated for IgG, IgM, and IgA antibodies targeting Spike proteins of seven human coronaviruses using the Luminex-based LABScreen COVID PLUS assay. Neutralizing titers were determined by infecting ACE2-expressing cells with Spike-pseudotyped lentiviruses encoding Firefly Luciferase. Cell-to-cell fusion between GFP+, Spike-expressing cells and ACE2-expressing cells was determined by automated fluorescent microscopy and image analysis using custom ImageJ scripts. All data was analyzed using GraphPad Prism.

Results: We detected IgM, IgG, and IgA responses to SARS-CoV-2 Spike and IgG responses to common-cold coronaviruses in our panel. We found that pseudovirus neutralizing activity correlated best with IgM responses targeting SARS2-CoV-2 Spike. In addition, most HSC samples were able to limit cell-to-cell fusion to some degree, which was correlated with both Spike-specific IgG and IgM responses.

Conclusions: Antibodies generated from SARS-CoV-2 infection generate diverse antibody responses with diverse functions. Inhibiting cell-to-cell fusion might be an important function of antibodies and should be evaluated as a potential correlate of protection.

Oral Presentation 3

Title: CORONAVIRUS OC43 INHIBITS STRESS GRANULE FORMATION BY MULTIPLE MECHANISMS

Authors: S Dolliver, DA Khaperskyy

Affiliation: Dalhousie University, Department of Microbiology & Immunology

Introduction: Stress granules (SGs) are cytoplasmic condensates that form in cells under certain types of stress. Current evidence suggests that SGs are antiviral and many viruses inhibit SG formation. Coronaviruses are a family of positive-sense RNA viruses that circulate in the human population, causing mild common colds as well as severe and often fatal disease. Despite growing interest into the antiviral function of SGs, little research has focused on the role of SG formation during coronavirus infection.

Methods: Here, using cell culture infection model, we utilized immunofluorescence to visualize stress granule formation and western blotting to examine expression of viral proteins and proteins involved in cellular stress responses. RT-qPCR was used to examine expression of mRNAs encoding key players in the innate immune response and stress response pathways.

Results: We observed low levels of SG formation upon OC43 infection of transformed human embryonic kidney (HEK) 293A cells or primary immortalized human upper airway epithelial BEAS2B cells. Further investigation revealed that OC43 inhibits SG formation in infected cells even in response to exogenous stimuli such as treatment with sodium arsenite (a robust SG inducer that causes oxidative stress), UV light, or double stranded RNA. Phosphorylation of the eukaryotic translation initiation factor 2 alpha (eIF2α), which is an upstream signaling event leading to SG formation, was inhibited in infected cells. Furthermore, ectopic expression of OC43 non-structural protein 1 (Nsp1) or nucleoprotein (N) was sufficient to inhibit SG formation.

Conclusions: We demonstrate that OC43 virus blocks SG formation by at least 3 complementary mechanisms: inhibition of upstream signaling through attenuating eIF2α phosphorylation and downstream inhibition by 2 viral proteins (Nsp1 and N). Existence of multiple SG suppression mechanisms suggests that SG formation may represent important antiviral host defense mechanism that coronaviruses target to ensure efficient replication.

Oral Presentation 4

Title: Modified Two-Tiered Testing Enzyme Immunoassay Algorithm for Serologic Diagnosis of Lyme Disease

Authors: F Khan[1,2]; Z Allehebi[1,2]; Y Shabi[1,2]; I Davis[1,2]; T Hatchette[1,2]

Affiliation: Department of Pathology and Laboratory Medicine, Queen Elizabeth II Health Science Centre, Halifax, NS, Canada[1]; Dalhousie University, Halifax, NS, Canada[2]

Introduction: The Standard two tier testing algorithm (STTT) for Lyme disease (LD) serology is known to have poor sensitivity to detect early localized infection, but a sensitivity for detecting late infection of >99% with a specificity of 99.2% (98.3±99.6) (Waddell et al., 2016). Recently, the FDA has approved a modified two-tier testing algorithm (MTTT) using two enzyme immunoassays (EIAs) which has been endorsed by the CDC and IDSA. We recently showed an MTTT using a whole cell EIA followed by C6 peptide EIA identified 25% more early LD cases than the STTT, with a specificity of 99.56%. Unfortunately, the company Immunetics stopped production of the C6 EIA which required us to validate two new EIAs to be used in the MTTT.

Methods: From March to July 2020, all patient specimens submitted for LD serology that were positive or indeterminate on the Zeus C10/VlsE EIA (ZEUS ELISA *Borrelia* VlsE1/pepC10 IgG/IgM) were tested with the Zeus whole cell EIA (ZEUS ELISA *Borrelia burgdorferi* IgG/IgM) (the MTTT) in addition to being sent to the National Microbiology Lab for immunoblot (IB) testing (the STTT). An attempt was then made to contact the ordering physicians to obtain clinical information that was used to determine whether the patient's clinical presentation was consistent with LD. Patients were classified as having "true LD" if they had: 1) a positive IgG IB, 2) a negative IgG and positive or negative IgM IB, but with any signs or symptoms consistent with early LD, or 3) evidence of seroconversion between consecutive specimens.

Results: Of 2196 specimens tested for LD, 241 were C10/VlsE positive. Of those, 197 had a WCS EIA done and 142 were positive. Clinical information was able to be obtained from ordering physicians for 87 patients from these 142 samples. Of the 55 patients not reviewed, 38 were IgG IB positive. Of the 87 patients reviewed, 8 where considered false positives with no clinical syndrome compatible with LD, 71 patients had early localized/early disseminated LD and 20 did not have positive IgM or IgG IB suggesting the MTTT has an increased sensitivity of 28% over the STTT. Considering that only 8 of 2196 would be considered false positive, there is a specificity of 99.6% (99.2%-99.8%).

Conclusions: The MTTT using the Zeus C10/VlsE EIA followed by the Zeus WCS improves the sensitivity for detection of early LD and has equivalent specificity to the STTT. Once the SOPs and training are established, we will be instituting this method for the serologic diagnosis of LD in NS tentatively targeting a start date of April 1, 2021.

Oral Presentation 5

Title: EVALUATION OF POP-UP ASYMPTOMATIC COVID-19 RAPID TESTING EVENTS IN NOVA SCOTIA

Authors: L MacDonald[1], B Goodall [1], S Meeker[1], S Davis [1,2], K Fraser [1], S Fraser [1], L Barrett [1,2], T Hatchette [1,2]

Affiliation: [1]Nova Scotia Health Authority (NSHA), Halifax, NS; [2]Dalhousie University, Halifax

Introduction: In fall of 2020, Nova Scotia entered its second wave of COVID-19. Community spread was linked to dine-in bar and restaurant settings in Halifax Regional Municipality (HRM), specifically in the 18–35-year-old demographic. To better assess for asymptomatic community spread, broad pop-up asymptomatic testing events were launched in late November, using the Abbott Panbio™ COVID-19 Antigen Rapid Test. Volunteers from the community were trained day-of to fill non-regulated care roles: screening, registering, and swabbing testing event attendees, testing the sample, delivering notification of results, and recording of results. Any attendees who received a positive test result were asked to return to the testing event to be swabbed again for a confirmatory PCR COVID-19 test and told to self-isolate. We evaluated the feasibility of the testing model as a community-based tool to supplement symptomatic testing delivered by Nova Scotia Health Authority.

Methods: Feasibility was evaluated retrospectively by reviewing the throughput and post-test surveys completed by event attendees as outcomes of the testing model.

Results: On average, 5-10 new non-regulated care providers are successfully trained to use rapid point of care tests at each pop-up event. 99 events have been held in communities across Nova Scotia between November 2020 and March 2021. 28,782 rapid tests have been conducted in this time, resulting in 13 laboratory confirmed positive tests. Non-regulated care providers report feeling empowered and comfortable in their roles, and attendees reported satisfaction and gratitude for the events.

Conclusions: The testing events have identified 13 asymptomatic individuals who were able to self-isolate, and thus did not inadvertently spread the virus in their community. Trained day-of, non-regulated care providers play a direct role in the success of these events. Their role reduces the burden on health care resources, enabling a broad, on-demand testing strategy, building testing capacity in communities across the province. In turn, the events allow for more community engagement in testing across Nova Scotia, promoting increased awareness of the importance of testing, reducing stigma by including testing of low-risk individuals to the provincial testing strategy, and informs Public Health officials of the extent of potential community spread. The essential role of non-regulated care providers illustrates the importance of their engagement for continued success in testing events.

Oral Presentation 6

Title: NKR-P1B SIGNALING IS REQUIRED FOR RESIDENT ALVEOLAR MACROPHAGE LIPID METABOLISM AND PROTECTION FROM BACTERIAL PNEUMONIA

Authors: M Scur, MMA Rahim, AB Mahmoud, B Parsons, F Abdalbari, I Stylianides, A Stueck AP Makrigiannis

Affiliation: Department of Microbiology and Immunology, Dalhousie University

Introduction: NKR-P1B is an inhibitory C-type lectin-like NK cell receptor. Its ligand, Clr-b, is a member of the C-type lectin-related ligand family. Expression and function of NKR-P1B:Clr-b axis in the context of myeloid derived immune cells has not been previously explored.

Methods: Flow cytometric and confocal analysis determined the effect of NKR-P1B ablation on alveolar macrophages (AMs), which we found to express NKR-P1B. Histology and lipidomic techniques are used to analyze AM lipid metabolic function and morphology. *In vivo* models utilizing *S. pneumoniae* and influenza were used to determine AM response to infection. Finally, *in vitro* assays and RNAseq were used to determine the extent of AM differentiation and functional impairment due to NKR-P1B ablation.

Results: Analysis of lungs from *nkrp1b*$^{-/-}$ mice revealed a collapse in AM numbers starting at 4 weeks of age. The lungs of healthy 6-week-old *nkrp1b*$^{-/-}$ mice are almost completely devoid of AMs. Monocytes repopulate the AM niche in a CCR2 dependent manner starting at 8 weeks of age and are present in significant numbers at 12 weeks of age. Surprisingly, AM numbers were found to be similar to WT controls in *Clr-b*$^{-/-}$ mice. Both the resident AM population prior to collapse, and reconstituted AMs in older *nkrp1b*$^{-/-}$ mice show a dysregulated CD11b^{hi} and F4/80^{lo} phenotype, suggesting a developmental arrest prior to terminal differentiation. Microscopic analysis of NKR-P1B-deficient lungs and isolated AMs shows a time-dependent presence of large, lipid filled cells suggesting an inability of AMs to degrade phagocytized pulmonary surfactant. Moreover, *nkrp1b*$^{-/-}$ mice are highly susceptible to pneumococcal infection, which could be related to AM disruption in these mice. Preliminary evidence through NKR-P1B tetramer staining in *Clr-b*$^{-/-}$ mice reveals possible alternative ligand for NKR-P1B.

Conclusions: The work presented here sheds light on a new role of NKR-P1B in the development and function of the lung AM population.

Oral Presentation 7

Title: CLR-F EXPRSSION REGULATES KIDNEY IMMUNE AND METABOLIC HOMEOSTASIS.

Authors: BD Parsons[1], HS Zein[1], E Abou-Samra[2], M Scur[1], C Hall[2], T Aboujamel[3], D Medina-Luna[1], G Gamage[1], MMA Rahim[5], A Steinle[5], AP Makrigiannis[1]

Affiliation: [1]Dept. of Microbiology and Immunology, Dalhousie University, Halifax Canada. [2]Dept. of Biochemistry, Microbiology, and Immunology, University of Ottawa, Ottawa Canada. [3]Dept. of Medical Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah Saudi Arabia. [4]Dept. of Biomedical Sciences, University of Windsor, Windsor Canada. [5]Institute for Molecular Medicine, Goethe University, Frankfurt am Main, Germany.

Introduction: The constitutive expression of the C-type lectin-related protein, Clr-f, in the kidney and intestinal epithelium is believed to act as a marker of health in these tissues; however, Clr-f is otherwise poorly defined. We generated a Clr-f deficient mouse to further characterize the tissue specific roles of Clr-f in vivo.

Methods: By targeted deletions in the *Clr-f* gene, we generated a Clr-f deficient mouse (Clr-f $^{-/-}$). Clr-f $^{-/-}$ kidney tissues were assessed by blind examination of histological and electron transmission microscopy. Kidney function was assessed by measures of urine and plasma creatinine levels. Kidney transcriptional profiles were surveyed from RNA sequencing of wildtype and Clr-f $^{-/-}$ mice at 7, 13 and 24 weeks of age. Immunofluorescent microscopy and flow cytometry were used to characterize renal immune cell infiltration and presence of auto-reactive antibodies in the kidney. The role of T and B lymphocytes in Clr-f $^{-/-}$ kidney pathology was determined using Rag-1-deficient mice Rag$^{-/-}$Clr-f $^{-/-}$ mice.

Results: Clr-f $^{-/-}$ mice have increased glomerular and tubular lesions, decreased kidney function and significant abdominal and ectopic lipid accumulation compared to wildtype mice. We detected IgM, IgA and IgG antibodies and increased C3 complement protein in the kidney of Clr-f $^{-/-}$ mice. Transcriptional profiling of Clr-f $^{-/-}$ mouse kidneys revealed dysregulation in the expression of inflammatory and metabolic genes. We detected increased IL-12 and IFN$_{\gamma}$ in Clr-f $^{-/-}$ mouse kidneys, and a significant presence of neutrophils and T and B lymphocytes and periglomerular leukocyte accumulation, that was exacerbated in Rag$^{-/-}$Clr-f $^{-/-}$ mice.

Conclusions: Clr-f exhibits tissue specific roles in immune and metabolic homeostasis of the kidney. The autoimmune pathology observed in Clr-f $^{-/-}$ kidneys supports a model of Clr-f as an indicator health, such that its loss releases constraints that prevent autoimmune reactivity. The pronounced lipid metabolic dysregulation in Clr-f $^{-/-}$mice points to an alternate homeostatic mechanism mediated by Clr-f in the kidney.

Oral Presentation 8

Title: DEFERRING RISK: HEALTHCARE PROVIDER RESPONSES TO THE USE IN PREGNANCY SECTION IN VACCINE PRODUCT MONOGRAPHS.

Authors: T Manca, K Top, K Weagle, J Graham

Affiliation: Canadian Center for Vaccinology, IWK Health Centre; Department of Pediatrics, Dalhousie University

Introduction: Vaccine product monographs (PMs) are not regularly updated and include a more limited scope of evidence than National Advisory Committee on Immunization (NACI) recommendations for vaccination in pregnancy. This inconsistent messaging from Health Canada, Industry Sponsors, and NACI contributes to misunderstandings and defers responsibility for vaccine safety to pregnant people and their healthcare providers (HCPs). In this paper, we discuss vaccine stakeholders and Canadian HCPs' responses to PMs.

Methods: Using a mixed methods approach, we started with a 2-day consensus workshop with vaccine stakeholders and HCPs. Stakeholders identified substantial limitations in the evidence in and purpose of vaccine PMs. Applying qualitative content analysis to the workshop transcripts, we then designed a national survey that included questions about HCP knowledge of vaccine PMs. Qualitative and quantitative descriptive statistics were further analyzed.

Results: Workshop stakeholders (N=27) identified the need for regular updating of evidence for vaccine safety and efficacy in PMs. Our national survey (N=367) showed that many HCPs were unfamiliar with the purpose of PMs and the limitations of the information in them. Only 36% knew that PMs do not regularly update information and 31% knew that PMs have different data than NACI uses for its recommendations.

Conclusions: Most HCPs are unaware of the limitations in the evidence in vaccine PMs and they may not use PMs as intended. We recommend that Health Canada require manufacturers to update PMs regularly. This is particularly important given the new adaptive clinical trial and expedited review regulations. Rapidly evolving safety data regarding vaccination in pregnancy will become available from ongoing surveillance for adverse events following immunization with COVID-19 vaccines. We conclude with a discussion of inconsistent messaging by government and industry that points to deferral of responsibility for assessing safety of off-label vaccine use onto individuals and their HCPs.

Oral Presentation 9

Title: COVID BELIEFS, BEHAVIOURS AND ANXIETY AMONG NON-ATLANTIC UNIVERSITY STUDENTS RETURNING TO NOVA SCOTIA

Authors: S Davis, B Goodall, S Meeker, L MacDonald, K Fraser, S Fraser, S Oldford, L Barrett

Affiliation: Dalhousie University, Halifax, NS, Canada

Introduction: University campuses are tight knit communities with students from across the globe and communal living arrangements. Combined behaviour-based prevention and screening efforts are required to reduce transmission of COVID-19. As provinces begin to reopen during the COVID-19 pandemic, guidelines and policies are in place to protect the public. However, individual adherence is crucial to reducing transmission. Behaviours are motivated by beliefs, including predicted disease severity. We examine student's COVID-19 anxiety levels related to their health protective behaviours and beliefs. Further, we identify concerns and barriers to self-isolation.

Methods: All Saint Francis Xavier (StFX) and Acadia university students returning to Nova Scotia (NS) in August into September 2020 were required to self-isolate for 14 days, have 3 COVID-19 swabs and complete 3 questionnaires. Questionnaire variables evaluated: demographics, beliefs, experiences, and anxiety related to COVID-19. Concerns with self-isolation were categorized through thematic analysis.

Results: 1050 (56% female) students (19 ± 2.26 years) completed the first questionnaire: 56% live off campus, 55% in first or second year, and 89% from Canada (59% Ontario). If infected, 10% predicted asymptomatic infection, 57% mild, 27% moderate, and 6% severe illness. Coronavirus anxiety scores indicated 78% had no anxiety, 22% some anxiety, and 0.4% dysfunctional anxiety. Students with moderate predicted illness severity had higher anxiety levels than those who predicted mild symptoms or asymptomatic ($X^2(3)=17.58$, $p<0.05$). Most respondents (>88%) agreed with health protective behaviours (physical distancing, masks, and hand washing). Common concerns with self-isolation included mental health, outdoor time, and food access.

Conclusions: University students returning to NS generally believe in and are compliant with health protective behaviours. They have low COVID-19 anxiety, and asymptomatic infection prevalence was underestimated. While many agreed with self-isolation and serial COVID-19 testing, there were concerns raised. Modifications to procedures surrounding COVID-19 mitigation strategies are essential moving forward to improve compliance and minimize harms to those returning to NS during the pandemic.

Oral Presentation 10

Title: REPEATED, LOW DOSE *CHLAMYDIA* INFECTIONS TRIGGER ABERRANT IMMUNE RESPONSES AND ENHANCED TISSUE PATHOLOGY

Authors: M Surette, M Tillman, A Mayavannan, J Wang

Affiliation: Department of Microbiology and Immunology, Dalhousie University

Introduction: *Chlamydia trachomatis* (*Ct*) infections severely impact women's health due to pelvic inflammatory disease (PID), and, for unclear reasons, repeated infections are correlated with severity. Contributions from animal studies, using a single inoculation, have imparted valuable findings, but utilizing a repeated infection model could expand the understanding of *Ct* driven tissue damage. We hypothesize that, compared to single infections, repeated *Chlamydia* infection dysregulates the immune response, and results in more severe pathology.

Methods: We inoculated mice with *C. muridarum* (*Cm*) using the conventional, single dose (1 dose of $6*10^5$ IFU; 1X), or repeated, low dose infections with the same cumulative number of bacteria (5 doses of $1.2*10^5$ IFU; 5X), and assessed the cellular, molecular, and pathology indicators of their immune response on days 10, 23, and 30 post-initial infection.

Results: Following 5X infection, pathology severity, indicated by oviduct cyst diameter, was significantly increased compared to the 1X group. This increase was associated with significantly elevated neutrophilic influx and pro-inflammatory cyto/chemokine concentrations in the genital tracts of 5X, but not 1X, infected animals, denoting differential host responses. IgG1 levels were markedly higher in the 5X group, while IgG2a levels were significantly higher in the 1X group, suggesting a skewed Th2 response in the 5X group, indicating a potential mechanism of pathology development following repeated infections. Differences in bacterial burden did not account for these differences, as both groups had similar levels of bacterial shedding.

Conclusions: Repeated *Cm* exposure induces a distinct molecular response, triggering maladaptive neutrophil recruitment, leading to a pathogenic modulation of T helper responses that promote tissue damage. These findings demonstrate the potential of repeated infection models to provide insight into the immune and pathology states in humans, and may be of value in elucidating, and targeting interventions to, host mediators of tissue damage during *Ct* infection.

Poster Abstracts

(Presenter's name in **bold)**

Poster 1

Title: CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS ADMITTED TO CANADIAN HOSPITALS WITH COVID-19: A REPORT FROM THE CANADIAN IMMUNIZATION RESEARCH NETWORK (CIRN) SERIOUS OUTCOMES SURVEILLANCE NETWORK

Authors: MK Andrew, J Godin, J LeBlanc, G Boivin, L Valiquette, A McGeer, JE McElhaney, TF Hatchette, M ElSherif, D McKinnon-Cameron, A Ambrose, S Trottier, M Loeb, K Katz, A McCarthy, **SA McNeil**

Affiliation: Department of Medicine, Divisions of Geriatric Medicine and Infectious Diseases

Introduction: COVID-19 has resulted in many hospitalizations across Canada. The Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network has been conducting active surveillance for influenza for the past decade and has pivoted to COVID-19 surveillance. Here we report characteristics and outcomes of adults admitted to SOS Network hospitals with COVID-19 between March and October 2020.

Methods: Prospectively enrolled cohort of all adult patients (aged 16+) admitted to ten SOS sites in Ontario, Quebec and Nova Scotia with positive COVID-19 test dates between February 28 and September 30th. Age, sex, demographics, housing, exposure characteristics, Clinical Frailty Scale, and comorbidities were collected. Outcomes included length of stay, intensive care unit (ICU) admission, mechanical ventilation and survival. Descriptive analyses and multivariable regressions were conducted.

Results: Among 745 patients with laboratory-confirmed COVID-19, mean age was 69 (range 20-105) years. 49.3% were women and 81.2% were Caucasian. 23.6% were admitted from Assisted Living facilities, 10.4% from long term care, and 2.1% from homeless shelters. The full spectrum of frailty was represented, and the majority had at least one underlying comorbidity. Mortality was 19.7% among those not admitted to ICU, and 28.5% for those admitted to ICU. Older age and higher frailty were associated with reduced ICU admission and increased mortality. Underlying comorbidities were not independently associated with adverse outcomes.

Conclusions: Early Canadian experience with hospitalized COVID-19 demonstrates the importance of frailty and age as independent predictors of lower ICU use and higher mortality. Even so, severe outcomes also occurred in younger and fitter patients. Continued surveillance will be critical to informing Canada's COVID-19 response, including eventual monitoring of vaccine effectiveness.

Poster 2

Title: HOW DOES FRAILTY IMPACT THE EFFICACY, REACTOGENICITY, IMMUNOGENICITY AND SAFETY OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE? A SECONDARY ANALYSIS OF THE ZOE-50 AND ZOE-70 STUDIES.

Authors: MK Andrew, JH Kim, S Matthews, C Dessart, MJ Levin, L Oostvogels, ME Riley, KE Schmader, SA McNeil, AE Schuind, D Curran

Affiliation: Department of Medicine, Divisions of Geriatric Medicine and Infectious Diseases

Introduction: Herpes zoster can negatively impact older adults' health and quality of life. An adjuvanted recombinant zoster vaccine (RZV) has excellent vaccine efficacy (VE), including in older adults. Given that frailty is strongly associated with vulnerability to illness and adverse health outcomes, we studied how frailty impacts RZV VE, immunogenicity, reactogenicity, and safety.

Methods: In the ZOE-50 and ZOE-70 pivotal Phase 3 efficacy studies of RZV, 29,305 participants aged 50-96 received 2 doses of RZV vs. placebo in 1:1 randomization. In this secondary analysis (NCT03563183), a baseline frailty index (FI) was created retrospectively following previously validated methods using pre-existing comorbidities and patient reported outcomes. Participants were categorized as non-frail (FI≤0.08), pre-frail (FI=0.08-0.25) or frail (FI≥0.25) for stratified analyses.

Results: FI was calculated for 99.8% of participants included in this secondary analysis (n=26,976) and was balanced between RZV and placebo groups. 45.6% were pre-frail and 11.3% were frail. Mean age was 68.8 years; 58.1% were women. RZV VE against HZ was consistently above 90% for all frailty categories [non-frail: 95.8% (95%CI: 91.6-98.2), pre-frail: 90.4% (84.4-94.4), frail: 90.2% (75.4-97.0)]. The RZV group demonstrated robust antibody responses post-dose 2 across frailty categories. In the RZV group, the percentage of participants reporting solicited adverse events decreased with increasing frailty. Unsolicited medically attended visits and serious adverse events increased with frailty and were balanced between placebo and RZV groups.

Conclusions: The ZOE studies included older adults who were frail and pre-frail, and VE was high across frailty categories. Reactogenicity decreased with increasing frailty, and no safety concerns were identified in any frailty group. An added feature of this study is that we demonstrated that a frailty index was readily calculated based on data often collected in randomized trials for vaccines and other interventions. Frailty could thus be considered retrospectively in other studies even where a frailty measure was not included up front. This study also provides an interesting example of how investigator-initiated questions can be addressed in partnership with Industry.

Poster 3

Title: EVALUATING IMPACT OF INCORPORATING CLINICAL PRACTICE GUIDELINES FOR MANAGEMENT OF INFECTIOUS DISEASES INTO AN ELECTRONIC APPLICATION (APP).

Authors: E Black[1,2], K Slayter[1,2], H MacKinnon[1,2], J Comeau[1,2]

Affiliation: [1]Dalhousie University, [2]IWK Health

Introduction: In 2017, locally developed evidence-based guidelines for infectious syndromes, pathogens and antimicrobials were established at our institution. To improve dissemination and accessibility of these guidelines to health care providers they were subsequently incorporated into the IWK Spectrum electronic application (App)**.** The objective of this study is to compare empiric antimicrobial prescribing before and after implementation of the App.

Methods: This study was completed as a retrospective chart review before and after implementation of the IWK Spectrum App. Pediatric patients admitted to IWK Health who were empirically prescribed an antibiotic for an infectious syndrome listed in the App were considered for inclusion. Prescribing was independently assessed by two members of the research team considering patient specific characteristics using a standardized checklist previously created by our group via the Delphi method. Assessment of antimicrobial prescribing was compared, and discrepancies were resolved through discussion. Results were reported using descriptive statistics. Interrupted time-series analysis is being completed.

Results: A total of 238 patients were included in the pre-implementation arm and 243 patients were included in the post-implementation arm. Empiric antimicrobial use was considered optimal in 81.9% (195/238) of patient's pre-implementation as compared to 93.0% (226/243) of patient's post-implementation.

Conclusions: An increase in appropriate empiric antimicrobial prescribing for pediatric patients with infectious syndromes was observed after implementation of an electronic App that included locally developed evidence based clinical practice guidelines. Use of electronic Apps may be an effective antimicrobial stewardship strategy to improve antimicrobial use in other patient populations. Further research to explore impact of an electronic App on patient outcomes is needed.

Poster 4

Title: PATIENT OUTCOMES OF A PRAGMATIC AND ADAPTIVE COVID-19 TREATMENT CLINICAL TRIAL

Authors: K Fraser, B Goodall, S Meeker, L MacDonald, S Fraser, S Oldford, L Barrett, T Ramsey, L Johnston, S McNeil, M Robbins, W Schlech, I Davis, P Bonnar, M Andrew, E Cameron, T Hatchette, D Haldane, G Patriquin, J LeBlanc, T O'Leary, O Loubani, R Green, K Rockwood, S Burgess

Affiliation: Dalhousie University, Halifax NS, Canada

Introduction: Since the COVID-19 pandemic began, it has been crucial to rapidly find effective treatments for those afflicted with acute COVID-19 symptoms. A pragmatic and adaptive approach was used for the COVID-19 treatment research study, because it offers patients the most up-to-date level of care. This approach gives clinician scientists the flexibility to change their protocol based on emerging data, so they are not restricted by the regulations of randomized controlled trials (RTCs). In this study, the COVID-19 therapeutic treatments changed based on recommendations from the World Health Organization (WHO) and medication availability. Various health outcomes were monitored in hospitalized COVID-19 patients to elucidate treatment efficacy of different study medications. A relationship between a treatment and an outcome will direct scientists and physicians on how to further treat the COVID-19 virus. Outcomes were measured relative to the treatments that patients received. Outcomes included the length of patients' hospital stay, patients' frailty levels, and intubation requirements.

Methods: Participants were recruited if they were hospitalized with acute symptoms of COVID-19. They were screened, consented, and assigned to a study medication or the clinical standard of care. Participants were assigned to a medication if they met eligibility criteria to take the study drug. The study medications used were baricitinib and hydroxychloroquine. Clinician scientists evaluated participants' frailty scales to measure their vulnerability to illness and ability to perform daily activities. Research staff obtained medical records to document their hospital stay, intubation status, and laboratory values.

Results: There were 12 participants enrolled in the COVID-19 treatment study from the Halifax Infirmary, Dartmouth General, and Valley Regional hospital. 2 participants were treated with hydroxychloroquine, 4 were treated with baricitinib, and 6 were treated with the clinical standard of care. There was no relationship observed between treatment type and participants' frailty. One participant received the highest frailty score, which was 8, meaning the participant was severely frail and dependent on others for personal care. Several other participants received the lowest frailty score of 1, meaning the participant was at the desired level of fitness for their age group. Hospital stay lengths varied from 5 to 29 days. The longest time that a participant stayed in the hospital was 48 days, and the shortest time was 3 days. No relationship was observed between treatment type and the length of hospital stay. One participant passed away while enrolled in the study, but it was not related to the administration of the study drug. Three participants required intubation at various points during their hospital admission. Two of those participants received the clinical standard of care as treatment and the other participant was being treated with baricitinib; this gave no indication that there was a relationship between intubated participants and their respective treatments.

Conclusions: To provide the best care for COVID-19 hospitalized patients, clinician scientists and physicians must understand the efficacy of novel treatments by monitoring patient outcomes for those on study medications versus the clinical standard of care. Based on this study, there was no significant relationship between study medication and the clinical standard of care as treatment. It can be noted the small sample size

of this study limits the ability to draw generalizable conclusions about the treatments. Therefore, it is pertinent to further investigate outcomes of hospitalized patients being treated for COVID-19.

Poster 5

Title: PEER-TESTERS FOR COVID-19 AS A POTENTIAL AID IN WIDESPREAD TESTING.

Authors: S Meeker[1], B Goodall[1], L Macdonald[1], K Fraser[1], S Fraser[1], S Fraser[1,2], T Hatchette[1,2], L Barrett[1,2]

Affiliation: [1]Nova Scotia Health Authority (NSHA), Halifax, NS; [2]Dalhousie University, Halifax

Introduction: Testing is an essential tool in reducing the spread of COVID-19. Understanding the effectiveness and acceptability of a new and engaged workforce (peer-testers) to lessen the burden on the usual care staff (RNs) that are already resource limited is important for developing sustainable and achievable operational procedures for future widespread testing.

Methods: In Fall 2020, students attending Acadia University or St. Francis Xavier University from outside the Atlantic bubble were required by the N.S. government to complete a COVID test and a corresponding survey at three time points during their isolation period. The students were asked to rate their experiences during the testing process. Results regarding their comfort level and opinions on receiving a test from peer-testers or regulated staff members were compiled. Peer-testers were hired and trained to administer the nasopharyngeal COVID test alongside regulated health care providers. The nurse educators and peer testers were interviewed on their opinions of the peer-testing role. The timeline of this initiative spanned four weeks, with a rapid roll-out.

Results: Over 75% of those surveyed identified a preference for a more casual testing experience (n=1015). Over 50% of the students identified as being tested by a peer-tester, 10% of students reported they were not tested by a peer-tester, and 39% were unsure who tested them (n=1015). All responses expressed a comparable rating when asked “What was your experience with having a COVID-19 swab?” with 28-36% rating the experience as ‘comfortable’ and 42-52% rating the experience as ‘uncomfortable’. There were 80 peer-testers recruited through student union engagement and social media, and 44 hired within three days. Despite obstacles inherent to rapid event roll-out, the nurse educators concluded that training the peer testers was a success. The peer testers reported a high degree of confidence quickly after being trained. They expressed personal achievements and positive interactions with the students in their daily feedback forms. Identified challenges included the unique nature of the testing environment which were stationed in dorm rooms.

Conclusions: The survey demonstrated that there were no negative implications from using unregulated testers. Data indicated that students preferred a casual testing experience, which peer-testers helped facilitate. These non-regulated professionals were shown to be useful to enhance testing capacity and diminish the burden on regulated providers, as demonstrated by the rapid recruitment and training period of this project. The implication from this project can be applied to similar populations, such as corrections facilities or long-term care.

Poster 6

Title: OPTIMIZING THE TREATMENT OF *STAPHYLOCOCCUS AUREUS* BLOODSTREAM INFECTION WITH THE IMPLEMENTATION OF A MOLECULAR ASSAY AND ANTIMICROBIAL STEWARDSHIP INTERVENTION

Authors: EK Reid[1], H Al Sidairi[2,3], N Sandila[4], J LeBlanc[1,2], I Davis[1,2], PE. Bonnar[1,2]

Affiliation: [1]Nova Scotia Health and [2]Dalhousie University, Halifax, NS; [3]Ibri Referral Hospital, Ministry of Health, Ibri, Oman; [4]Research Methods Unit, Nova Scotia Health, Halifax, NS

Introduction: Vancomycin is often used for *S. aureus* bloodstream infections pending sensitivities. Earlier sensitivity reporting should decrease vancomycin use and optimize early beta-lactam antibiotic therapy in patients with methicillin-susceptible *S. aureus* (MSSA) infections. We assessed the impact of implementing Xpert® MRSA/SA BC (Cepheid) molecular testing coupled with an antimicrobial stewardship (AMS) intervention on the time to optimal antimicrobial therapy for *S. aureus* bloodstream infections.

Methods: Xpert® molecular testing was performed for patients with *S. aureus* bloodstream infections between January and July 2020. Using the determined sensitivity information, the AMS team contacted the treating physician with the results via phone and provided advice. The primary outcome of interest was time to optimal therapy, defined as the time from first blood culture draw to time of optimal therapy. Optimal therapy was defined as the first appropriately dosed cefazolin or cloxacillin monotherapy, or the time at which vancomycin concomitant to cefazolin or cloxacillin was discontinued. The outcome was compared with a historical cohort from 2017-2018.

Results: 56 patients (29 intervention, 27 control) were included. The median time to optimal therapy was shorter in the intervention group compared to the historical cohort (38.0 hours, 95% CI 32.8, 47.0, vs. 50.1 hours, 95% CI 29.8, 69.5). Time to optimal therapy was characterized using Kaplan-Meier plots, and the log-rank test indicated that the curves differed significantly by group ($p = 0.0405$). Participants in the intervention group at any time point during the study period were 77% more likely to start optimal therapy (HR 1.77, 95% CI 1.02, 3.09, $p = 0.0432$).

Conclusions: Implementing Xpert® molecular testing with AMS notification significantly reduced the time to optimal therapy in patients with MSSA bloodstream infections. Implementing molecular testing, particularly in remote hospitals where there may be delays in sensitivity testing, can improve therapy optimization and contribute to improved patient outcomes.

Poster 7

Title: TLR2 SIGNALLING IS ESSENTIAL FOR STEERING A PROTECTIVE IMMUNE RESPONSE AND CONTROLLING PATHOLOGY UPON *CHLAMYDIA* GENITAL TRACT INFECTION

Authors: A Mayavannan[1,4], E Shantz[1,4], JS Marshall[1,3], J Wang[1,2,4]

Affiliation: [1]Department of Microbiology and Immunology, [2]Department of Pediatrics, [3]Department of Pathology and [4]Canadian Centre for Vaccinology

Introduction: *Chlamydia* is a bacterial STI that causes severe reproductive tract complications in women. Toll-Like Receptor 2 (TLR2) is a pathogen sensing receptor ubiquitously expressed in host tissues including lymphoid and non-lymphoid organs. Certain TLR2 polymorphisms are known to confer risk for *Chlamydia* infection in women. However, the role of TLR2 in the immunopathogenesis of *Chlamydia* is not well elucidated.

Methods: To characterize the role of TLR2 in host responses to *Chlamydia* infection, we infected $TLR2^{+/+}$ and $TLR2^{-/-}$ mice intra-vaginally with *Chlamydia muridarum* and characterized innate and adaptive immune responses and oviduct pathology at various time points. Cysts formed in the oviduct were comparable between the strains at 50-52 days post infection and the absence of TLR2 resulted in the formation of significantly larger cysts at 70-72 days post infection. The absence of TLR2 significantly dampened all T helper immune responses assessed at the earlier time point, but selectively promoted Type 2 response at the later time point. TLR2KO mice were incapable of producing a robust systemic Th17 immune response but IL-17A production was rescued in bone marrow chimeras reconstituted with TLR2+ bone marrow cells. To further elucidate the dysregulation of T cell cytokine responses, we examined antigen presenting cells and found TLR2KO mice have lower frequencies of splenic plasmacytoid dendritic cells and macrophages at baseline. Moving forward, we will be examining the role of TLR2 in dendritic and macrophage cell functions and their role in shaping adaptive, protective T cell responses and resolution of cysts.

Results: Preliminary work from our laboratories has shown human mast cells to produce several pro-inflammatory cytokines and chemokines in response to *Chlamydia trachomatis* (*Ct*) infection. Using a murine model, we have characterized these responses to be dependent on TLR2 signaling. To dissect the mechanism of interaction of *Ct* with human mast cells, mast cells were screened for genes that were either up-regulated or down-regulated by *Ct* infection using a PCR array. From the results, mast cells appeared to interact with *Ct* through TLR2 and produce pro-inflammatory mediators downstream of the NF-κB and MAPK pathways. Further experiments are underway to validate these potential mechanisms of mast cell-*Ct* interaction.

Conclusions: Collectively these results show that the engagement of TLR2 is crucial for steering protective immune responses and in controlling the development of chronic cysts in *Chlamydia* genital tract infection. Elucidating the functional role of TLR2 would help reduce reproductive tract complications in *Chlamydia* affected women.

Poster 8

Title: ADAPTIVE RESPONSES OF NATURAL KILLER CELLS EXHIBIT DISTINCT REQUIREMENTS AMONG MEMBERS OF THE LY49 RECEPTOR FAMILY.

Authors: G Gamage, D Medina-Luna, M Scur, H Zein, BD Parsons, MMA Rahim, AP Makrigiannis

Affiliation: Department of Microbiology and Immunology, Dalhousie University, Halifax, NS

Introduction: Immunological memory is a hallmark of the adaptive immune system. However, recent evidence revealed that natural killer (NK) cells, a subset of innate lymphoid cells, also mediate antigen-specific memory responses. Our lab previously identified the mouse NK cell receptors, Ly49C and/or Ly49I, as mediators of NK cell antigen-specific recall responses through their interaction with MHC-I ligands H-2K^{b} and H-2D^{b}. To better define the requirement for Ly49 receptors in NK cell memory, we investigated if other Ly49 receptors are also capable of mediating antigen-specific NK cell memory responses in the presence of their specific MHC-I ligands. Findings from this study will help demark new boundaries in our understanding of adaptive immunological memory, clarify NK cell roles in these memory responses and open opportunities to exploit NK cell memory for use in vaccine development and cancer immunotherapy.

Methods: We tested immunological memory responses to the chemical hapten, 2, 4 dinitrofluorobenzene (DNFB), and to the HIV-1 peptide, gp160, by contact hypersensitivity (CHS) ear swelling assays in mice. To specifically test the role of Ly49G in NK cell memory responses, we performed CHS ear swelling assays in mice that lack T and B lymphocytes (RagKO), Ly49G receptors, and congenic for the MHC-I haplotype H-2d (RagKO-Ly49GKO H-2d). We also tested Ly49C/I roles in adaptive NK cell responses, by selectively depleting NK cells that expressed Ly49C/I receptors, using antibody mediated depletion prior to the DNFB and gp160-induced CHS assay in RagKO mice congenic for MHC-I H-2d haplotype.

Results: Mice lacking Ly49G receptors showed no difference in ear swelling response to DNFB or gp160 compared to controls. However, ear swelling responses to DNFB and gp160 was significantly reduced in mice depleted of Ly49C/I-expressing NK cells.

Conclusions: Overall, our findings show that Ly49C/I can mediate adaptive NK cell memory by interacting with MHC-I ligands H-2D^{d}, H-2L^{d} and H-2K^{d}, thus illustrating a critical role of Ly49C/I receptor in adaptive NK cell memory. The presence of memory in mice lacking Ly49G receptors suggests that NK cell memory may be intrinsic to select Ly49 receptors, such as Ly49C/I. Thus, further studies are needed to define Ly49 receptors roles in NK cell memory responses.

Poster 9

Title: THIOPURINES ACTIVATE AN ANTIVIRAL UNFOLDED PROTEIN RESPONSE THAT BLOCKS INFLUENZA A VIRUS GLYCOPROTEIN ACCUMULATION

Authors: P Slaine[1], M Kleer[2], BA Duguay[1], ES Pringle[1], E Kadijk[1], S Ying[1], A Balgi[3], M Roberge[3], C McCormick[1], DA Khaperskyy[1]

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Introduction: Influenza A viruses (IAVs) use host cell machinery to synthesize viral proteins. Most viral mRNAs are translated by free ribosomes in the cytoplasm, whereas mRNAs encoding the viral glycoproteins hemagglutinin (HA) and neuraminidase (NA) are translated in the endoplasmic reticulum (ER) and traffic to the cell surface to participate in viral assembly and egress. We study two candidate antiviral thiopurines 6-thioguanine (6-TG) and 6-thioguanosine (6-TGo) that impede viral glycoprotein synthesis by activating the cellular unfolded protein response (UPR) that responds to the accumulation of misfolded proteins in the ER.

Methods: Lung adenocarcinoma A549 cells were infected with IAV (A/Puerto Rico/08/1934 (H1N1)) and treated with 6-TG and 6-TGo to determine effects on viral protein synthesis and replication. Infectious virions were enumerated by plaque assay. Viral proteins were analyzed by immunoblot. Viral mRNA synthesis and genome replication were measured by RT-qPCR. UPR was analyzed by immunoblot and RT-qPCR. Host responses were manipulated with chemical inhibitors and by CRISPR knockout of the UPR sensor kinase PERK.

Results: 6-TG and 6-TGo reduced viral titers by ~100-fold. While these thiopurines did not affect viral mRNA synthesis and genomic replication, we observed a marked decrease in viral glycoprotein processing and accumulation that correlated with activation of the UPR. UPR modulation via chemical chaperones partially restored viral glycoprotein processing and accumulation. PERK knockout or chemical inhibition of PERK-dependent downstream responses restored synthesis of viral proteins but they were not properly glycosylated.

Conclusions: We demonstrate for the first time that 6-TG and 6-TGo activate the UPR and inhibit IAV replication. This provides a new conceptual framework for host targeted antivirals.

Poster 10

Title: INVESTIGATING HOW CORONAVIRUSES SUBVERT THE UNFOLDED PROTEIN RESPONSE

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Not published by request.

Poster 11

Title: MOBILIZATION OF MEMORY NK CELLS IN CANCER IMMUNOTHERAPY

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Introduction: Immunological memory has long been attributed exclusively to T and B lymphocytes; however, we now know that natural killer (NK) cells also possess an analogous function. Studies of Rag-1-deficient mice ($Rag^{-/-}$), which lack T and B cells, provided evidence of NK cell-mediated immunological memory. As NK cells also possess a natural capacity to recognize and eliminate tumor cells, we set out to define the role of NK cell memory in anti-cancer immune responses using NK cell-targeted cancer immunotherapy through vaccination.

Methods: $Rag^{-/-}$ mice were immunized with the RAHNIVYTIF (R9F) peptide from the HPV virus, using the proprietary DepoVax (DPX) vaccine formulation, (IMV, Inc., Dartmouth, Canada). Sixteen days after immunization, mice were flank-injected with C3 tumor cells which express the R9F antigen. A control cohort of $Rag^{-/-}$ mice received DPX alone. Tumor appearance and tumor growth rates were recorded. To confirm the role of perforin in anti-tumor activity, we immunized perforin-deficient $Rag^{-/-}$ mice ($Rag^{-/-}$ $Prf^{-/-}$) with either DPX-R9F or DPX alone sixteen days prior to C3 tumor implantation.

Results: $Rag^{-/-}$ mice vaccinated with DPX-R9F had better protection against C3 tumor development, with 60% remaining tumor-free in comparison to the control cohort, in which all mice developed tumors. Additionally, the tumor growth rate in vaccinated mice was significantly slower than in the control cohort. This anti-tumor protection was dramatically reduced in $Rag^{-/-}$ $Prf^{-/-}$ mice, as only 20% of DPX-R9F-immunized mice remained tumor-free, and the tumor growth rate in $Rag^{-/-}$ $Prf^{-/-}$ mice was increased significantly compared to the $Rag^{-/-}$ control mice.

Conclusions: Our preliminary results suggest that DPX-R9F immunization induces protection against tumor development in mice in a T cell- and B cell-independent manner. Additionally, our results suggest that perforin is an essential anti-tumor effector molecule in the observed anti-tumor responses. Future cancer immunotherapies could be improved by priming not only T cells but also NK cells, providing better patient outcomes.

Poster 12

Title: INVESTIGATING THE MECHANISM OF ACTION OF A VIRAL BZIP TRANSCRIPTION FACTOR

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Introduction: Viral infections and endogenous dysregulations in cellular homeostasis cause unfolded proteins to accumulate inside the cell's endoplasmic reticulum (ER), causing ER stress. The cellular unfolded protein response (UPR) constitutes three distinctive arms that detect unfolded proteins and restores homeostasis by increasing folding capacity. Kaposi's sarcoma associated herpesvirus (KSHV) is a human oncovirus that causes Kaposi's sarcoma (KS) and other cancers. During lytic replication, KSHV activates the UPR to aid viral replication, but suppresses the antiviral downstream transcriptional responses aimed at relieving ER stress. These downstream responses are governed by basic leucine zipper (bZIP) proteins, which are transcription factors that bind DNA as homo- or heterodimers. KSHV encodes a viral bZIP, the multifunctional K-bZIP, early during lytic infection. Because bZIPs interact and dimerize with one another, we hypothesized that K-bZIP can bind the bZIPs of the UPR to inhibit target gene induction and promote efficient viral replication.

Methods: To assess if K-bZIP inhibits UPR target gene expression, lentiviruses expressing K-bZIP were generated. CHO-7.1 cells or HEK293A cells were transduced with K-bZIP and treated with thapsigargin to induce ER stress. Expression of UPR-responsive target genes representative of all three arms of the UPR was then assessed using flow cytometry or RT-qPCR. Lastly, to assess combinatorial effects of K-bZIP and its known viral interaction partners, ORFs 36, 50, and 57, on the transcriptional activity of the UPR bZIP activating transcription factor 6 (ATF6), HEK293T cells were co-transfected with K-bZIP and interaction partners. ATF6 activity was measured with an ATF6-inducible luciferase plasmid.

Results: K-bZIP did not inhibit the downstream transcriptional responses of any of the arms of the UPR alone or in combination with interaction partners.

Conclusions: The functions of K-bZIP during the lytic life cycle of KSHV do not involve UPR modulation.

Poster 13

Title: SARS-COV-2 IMMUNITY IN MODERATE TO SEVERE COVID-19 PATIENTS ENROLLED IN THE PRAGMATIC, ADAPTIVE CO-VIC COVID-19 TREATMENT STUDY

Authors: S Oldford[1,2], P Zanello Antunes[1], T Brauer-Chapin[1], L Barrett[1,2]

Affiliation: [1]Dalhousie University and [2]Nova Scotia Health Authority, Halifax, NS, Canada

Introduction: Clinical COVID-19 outcome is likely dependent on the degree of immune dysregulation, development of effective anti-viral immunity, and limited SARS-CoV-2 induced immunopathology. Current therapeutic strategies are focused on anti-viral and/or anti-inflammatory treatments. These therapeutics may differentially impact the development of SARS-CoV-2 specific immunity and clinical outcome. **Objective:** To describe cellular and humoral immunity in patients with moderate to severe COVID disease before and after COVID-19 treatment to determine correlates of improved clinical outcome.

Methods: Hospitalized COVID-19 patients enrolled in the CO-VIC treatment study are consented into an immunologic substudy. To date, 12 participants have been enrolled and 6 have received investigational therapy (4 baricitinib, 2 hydroxychloroquine sulfate) and 6 no adjunctive treatment. Peripheral blood samples are collected at baseline, during and end of treatment, and at 2 follow-up periods (d29 and d180). Activation and exhaustion in NK, T and B cell subsets is measured by flow cytometry. B cell IgG and IgA ELISPOT and T cell IFN-g ELISPOT measure global (common coronaviruses, H1N1 and CMV) and SARS-CoV-2 specific B and T cell function.

Results: SARS-CoV-2 infected hospitalized individuals display a marked decrease in peripheral blood mononuclear cells as compared to mild COVID-19 and uninfected individuals, primarily due to decreased CD8+ T cells. CD8+ T cells expressing the CD28 activation marker increased with both investigational and standard of care treatment. Dysfunctional B cell regulation was observed in severe COVID-19 with elevated tissue-like memory B cells. Preliminary T cell ELISPOT data demonstrate increased IFN-gamma responses against SARS-CoV-2 spike, membrane and nucleoprotein antigens through the course of treatment.

Conclusions: These data demonstrate that early SARS-CoV-2 specific T cell responses across major structural proteins are present in hospitalized patients and increase with treatment. Comprehensive characterization of global and SARS-CoV-2 cellular and humoral immunity in COVID-19 patients, correlating to viral persistence, disease severity and outcome, will provide important information on the immune response to SARS-CoV-2 and immune correlates of disease outcome.

Poster 14

Title: CMV COINFECTION AND T CELL EXHAUSTION IN LTCF RESIDENTS WITH COVID-19

Authors: S Oldford[1,2], P Zanello Antunes[1], T Brauer-Chapin[1], B Ray[1], L Barrett[1,2]

Affiliation: [1]Dalhousie University and [2]Nova Scotia Health Authority, Halifax, NS, Canada

Introduction: Elderly long-term care facility (LTCF) residents have been disproportionately affected by COVID-19 and have suffered significant mortality and morbidity. Correlates of immunologic protection and susceptibility are not defined in highly vulnerable, advanced age, cohorted populations such as in LTCF. Elderly individuals are also often co-infected with cytomegalovirus (CMV), which may impact SARS-CoV-2 immunity.

Methods: During a COVID-19 outbreak at a LTCF, peripheral blood was collected at baseline and 1 month from 108 LTCF residents, following informed consent. Peripheral blood mononuclear cells (PBMC) and plasma were isolated from whole blood samples. T and B cell immune subsets were examined by flow cytometry of whole blood. CMV co-infection was determined by in-house ELISA of plasma samples. T cell IFN-g ELISPOT using cryopreserved PBMC was used to measure SARS-CoV-2 specific T cell function.

Results: The cohort consists of highly exposed uninfected (n=48) and COVID-19 infected (n=60) LTCF residents. SARS-CoV-2 infection was more frequent in older females. 72% of individuals are CMV+ with no difference between COVID-19- and COVID-19+ individuals. However, COVID-19+ individuals <80 years old were more predominantly CMV+ (p=0.04). CMV+ LTCF residents exhibited increased markers of T cell exhaustion and senescence (CD57, PD-1, Tim-3) and decreased markers of activation (CD27, CD28) on CD4+ and CD8+ T cell subsets in both COVID-19- and COVID-19+ individuals. The most pronounced T cell exhaustion was observed in CMV+COVID-19+ individuals. COVID-19 recovered individuals showed decreased CD57+PD-1+Tim-3+CD4+ T cells (p=0.0147) and CD57+PD-1+Tim-3+CD8+ T cells (p=0.0212), 1 month later (N=13). Preliminary T cell ELISPOT data demonstrate less frequent and more limited breadth of T cell responses against SARS-CoV-2 spike, membrane and nucleoprotein antigens in exposed COVID-19- individuals (N=10) compared to COVID-19+ individuals (N=22). In COVID-19+ individuals, SARS-CoV-2 specific T cell IFNg responses did not significantly differ between CMV- and CMV+ individuals.

Conclusions: CMV infection increases T cell exhaustion in LTCF residents and may exacerbate T cell exhaustion in COVID-19. Further study is required to fully understand SARS-CoV-2 immunity in LTCF to inform rational COVID treatment and vaccination.

Poster 15

Title: DISEQUILIBRIUM OF THE VAGINAL MICROBIOME AS A PREDICTOR OF SEXUALLY TRANSMITTED INFECTION.

Authors: C Phillips[1,2], DJM Haldane[2,3]

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Introduction: Bacterial vaginosis is manifested by a disequilibrium of the vaginal microbiome which predisposes to acquisition of sexually transmitted infection (STI). We wondered if the presence of bacterial vaginosis should be a prompt for further testing for infection with chlamydia, gonorrhea, and trichomonas.

Methods: Bacterial vaginosis was diagnosed in patients between the ages of 15 and 49 by a gram stain of a vaginal smear using a scoring system that relates the presence or absence of bacterial morphotypes to define high risk of bacterial vaginosis (BV positive), intermediate risk (BV intermediate) and low risk (BV negative). Trichomonas infection was diagnosed by morphological identification using gram stain of the same vaginal smear, and chlamydia and gonorrhea were diagnosed by nucleic acid amplification testing (NAAT) on a separate vaginal swab. Laboratory records were reviewed for paired sample results, sent for gram stain and NAAT, sent on the same day between 2014 and 2019. The rates of positivity for high or intermediate risk of bacterial vaginosis and detection of *Trichomonas*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* were calculated and compared with the rates detected in samples showing a low risk for bacterial vaginosis.

Results: Of 59161 results of BV scoring, 25% were BV-positive, 15% were BV-intermediate and 60% were BV-negative. Approximately 70% of the vaginal gram stains were accompanied with NAAT tests. Of the BV negative samples, chlamydia and gonorrhea rates were 3.25% and 0.09 %, respectively. For the BV-positive/intermediate samples, chlamydia and gonorrhea rates were 6% and 0.35 %, respectively. Of all vaginal gram stains, 446 were positive for *Trichomonas:* 26% were BV-positive, 51% were BV-intermediate, 13% were BV-negative, and 10% were not scored as the patient was over the age of 50. Of trichomonas positive samples, 75 % had paired NAAT testing: 6% were positive for chlamydia, and 1.19% were positive for gonorrhea.

Conclusions: Limitations to these results are the lack of clinical data for symptoms, and microscopic detection of trichomonas is insensitive. While this study confirms the association between BV and trichomonas, chlamydial and gonorrhea infection, the presence of BV is insensitive as a screening tool for the presence of these infections.

Poster 16

Title: SAFETY AND IMMUNOGENICITY OF V114 ADMINISTERED CONCOMITANTLY WITH INFLUENZA VACCINE (PNEU-FLU)

Authors: R Severance[1], H Schwartz[2], M Davis[3], K Lesh[4], R Dagan[5], L Connor[6], J Li[6], A Pedley[6], J Hartzel[6], T Sterling[6], K Nolan[6], G Tamms[6], L Musey[6], U Buchwald[6], Presenter by **V. Racovitan**.

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Introduction: Streptococcus pneumoniae and influenza virus are significant causes of disease worldwide. V114, an investigational 15-valenl PCV, contains all serotypes in PCV13 plus serotypes 22F and 33F. This phase 3 trial evaluated safety and immunogenicity of concomitant and non-concomitant administration of V114 and quadrivalent influenza vaccine (QIV) in adults aged $\geq$50 years

Methods: Overall, 1200 participants were randomized 1:1 to receive either V114 administered concomitantly with QIV (concomitant group) or V114 administered 1 month after QIV (non-concomitant group); randomization was stratified by age and history of prior pneumococcal polysaccharide vaccine. Pneumococcal serotype-specific opsonophagocytic activity (OPA) and influenza strain-specific hemagglutination inhibition (HAI) antibodies were measured prior and 30 days postvaccination. Demonstration of non-inferior immunogenicity between the concomitant and non-concomitant group required the lower bound of the 95% confidence interval of the ratio of OPA and HAI geometric mean titers (GMTs) to be $\geq$0.5.

Results: Proportions of participants reporting any AE, injection-site AEs, and systemic AEs were generally comparable between vaccination groups. Non-inferiority was demonstrated for all 15 pneumococcal serotypes and all 4 influenza strains between vaccination groups.

Conclusions: V114 administered concomitantly with QIV was generally well tolerated and immunologically non-inferior to non-concomitant administration, supporting co-administration of both vaccines.

Poster 17

Title: SAFETY AND IMMUNOGENICITY OF V114, A 15-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV), IN ADULTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV): A PHASE 3 TRIAL

Authors: L Mohapi[1], O Osiyemi[2], K Supparatpinyo[3], W Ratanasuwan[4], JM Molina[5], R Dagan[6], G Tamms[7], T Sterling[7], Y Zhang[7], J Hartzel[7], A Pedley[7], Y Kan[7], K Hurtado[7], U Buchwald[7], L Musey[7], J Simon[7], Presented by **V. Racovitan**

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Introduction: HIV infection increases the risk of pneumococcal disease (PD). Sequential vaccination with PCV followed by 23- valent pneumococcal polysaccharide vaccine (PPSV23) has been recommended for prevention of PD in HIV-infected individuals. V114 is an investigational 15-valent PCV and contains all serotypes in PCV13, plus serotypes 22F and 33F. This phase 3 trial evaluated the immunogenicity and safety of V114 or PCV13 followed 8 weeks later by PPSV23 in HIV-infected adults.

Methods: Eligible HIV-infected adults aged ≥18 years, pneumococcal vaccine naive and receiving antiretroviral therapy were randomized 1: 1 to receive either V114 or PCV13 followed by PPSV23 8 weeks later. Randomization was stratified by CD4+ cell count. Serotype-specific opsonophagocytic activity (OPA) and immunoglobulin G (lgG) antibodies were measured immediately prior to V114/PCV13 and 30 days after each vaccination.

Results: 302 participants were randomized to receive V114 (n= 152) or PCV13 (n= 150). Of the participants, 78.8% were males; 72.2% were 18-49 years old; 98.7% had CD4+ T-cell count ≥200 cells/µL; and 51.7% had CD4+ T-cell count <500 cells/µL at screening in both intervention groups; 78.5% had undetectable HIV RNA. All vaccines were generally well tolerated, and safety profiles were generally comparable across vaccination groups. V114 and PCV13 induced OPA and lgG antibodies at 30 days post vaccination (Day 30) to all serotypes included in the respective vaccines. 30 days following administration of PPSV23, V114 and PCV13 OPA and lgG antibody levels were generally comparable to those observed at Day 30 after V114/PCV13 administration for serotypes in the respective PCVs. Geometric mean fold rises, percentages of subjects with ≥ 4-fold-rise from baseline, and reverse cumulative distribution curves for both OPA and lgG antibodies were consistent with an immune response that was generally comparable between V114 and PCV13 for shared serotypes.

Conclusions: In pneumococcal vaccine-naive adults infected with HIV, V114 followed 8 weeks later by PPSV23, as per recommendations aimed at prevention of PD in HIV-infected individuals, is generally well tolerated, induces immune responses for all 15 pneumococcal serotypes as assessed by OPA geometric mean titers and lgG geometric mean concentrations at 30 days after V114 and after PPSV23 administration.

Poster 18

Title: EVALUATING BARRIERS AND FACILITATORS TO DELIVERY OF HOSPITAL PHARMACY SERVICES TO WOMEN, CHILDREN AND THEIR FAMILIES DURING A PANDEMIC

Authors: E Ring[1,2], K Slayter[1,2], M MacInnis[1], JE Isenor[1,2], E Black[1,2]

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Introduction: When the first wave of COVID-19 emerged in March 2020, health care professionals across Canada were challenged to quickly and efficiently adapt to change their work practices. To our knowledge, efforts to systematically gather data on barriers and facilitators to delivery of hospital pharmacy services using an evidence informed approach has not been completed. The primary objective of our study was to identify and describe barriers and facilitators to delivering hospital pharmacy services to women, children, and their families during a pandemic.

Methods: This qualitative study was completed using semi-structured virtual interviews. Pharmacists that worked in direct or non-direct patient care throughout the pandemic (since March 2020) from Women's and/or Children's Hospitals in Canada were included. Individual interviews were completed virtually using Cisco Webex. An interview guide mapped to the Theoretical Domains Framework Version 2 (TDFV2) was used to facilitate interviews. Interviews were audio-recorded and transcribed verbatim by the principal investigator. Transcribed interviews were then coded, mapped to the TDFV2, and are being analyzed using thematic analysis.

Results: Twenty-one interviews were completed with pharmacists in seven provinces across Canada. The most commonly reported barriers or facilitators mapped to TDFV2 domains included ***Environmental Context and Resources*** such as personal protective equipment (PPE) and virtual care; ***Social/Professional Role and Identity*** including expanded scope of practice; and ***Emotion due to factors such as added stress from increased workload. Additional analysis of themes is ongoing.***

Conclusions: We identified barriers and facilitators associated with pharmacist delivery of hospital services. Understanding of these challenges can assist in the development of policies and initiatives to enhance pharmacy services and patient care during pandemics.

Poster 19

Title: THE UNRELIABILITY OF CASPOFUNGIN TESTING IN PREDICTING ECHINOCANDINSUSCEPTIBILITY AMONG CLINICAL ISOLATES OF CANDIDA GLABRATA

Authors: Y Shabi[1], A Russell-Tattrie[1], A Bharat[2], D Haldane[2], G Patriquin[1]

Affiliation: Dalhousie University, Halifax, NS, Canada[1]. National Microbiology Laboratory, Winnipeg, Manitoba, Canada[2]

Introduction: Clinical isolates of Candida species typically undergo susceptibility testing (to azoles and echinocandins). Multiple echinocandins are commercially available for in vitro susceptibility testing using an agar gradient diffusion method, including micafungin, caspofungin and anidulafungin. After institutional formulary (and therefore susceptibility testing) was changed from micafungin to caspofungin, we experienced an abrupt increase in echinocandin resistance among clinical isolates of C. glabrata. In this study, we determined and quantified discrepancies in echinocandin testing among three agents and found that caspofungin testing results had overestimated echinocandin resistance.

Methods: We queried the laboratory information system for caspofungin-resistant C. glabrata isolates, and retrospectively tested these isolates for sensitivity to micafungin and anidulafungin, using an agar diffusion method. We compared these results with those generated prior to the institutional change to caspofungin, and to those generated after adopting European Committee on Antimicrobial Susceptibility Testing (EUCAST) testing guidelines (inferring caspofungin sensitivity from a combination of results from micafungin and anidulafungin). The study period was a total of 44 weeks. Breakpoints were determined by Clinical & Laboratory Standards Institute (CLSI) guidelines. Descriptive statistics were used.

Results: A total of 44 C. glabrata isolates from various body sites were tested (mostly from sterile sites). The baseline echinocandin non-susceptibility rate prior to the change to caspofungin testing was 5.3% (n 19), which increased to 91.7% (n 12) coinciding with the change to caspofungin testing ($p < 0.0001$). Institution of EUCAST guidelines resulted in a return to baseline echinocandin non-susceptibility rates of 7.7% (n 13). Retrospective testing of micafungin/anidulafungin-sensitive isolateswith caspofungin confirmed erroneous detection of echinocandin resistance based on caspofungin MICs.

Conclusions: This study quantifies and emphasizes the unreliability of caspofungin testing by agar diffusion for determining echinocandin resistance in C. glabrata, which may affect patient management and antifungal choice.

Poster 20

Title: TREATMENT OF BLOODSTREAM INFECTIONS CAUSED BY CEFTRIAXONE-RESISTANT *E. COLI, P. MIRABILIS* AND *KLEBSIELLA* SPECIES: REVIEW OF EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCTION AND PATIENT OUTCOMES IN A LOW PREVALENCE SETTING

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Introduction: Invasive infections due to extended-spectrum beta-lactamase (ESBL) producing Enterobacterales may have reduced susceptibility to beta-lactam/beta-lactamase inhibitor (BLBLI) antibiotics, contributing to broad-spectrum carbapenem use. Recent Infectious Diseases Society of America guidelines recommend that carbapenem or non-BLBLI antibiotics be used preferentially in the treatment of non-cystitis ESBL infections, even in cases where BLBLI susceptibility is demonstrated through in vitro laboratory testing. We aimed to characterize the impact of ESBL production and antibiotic choice on clinical outcomes in patients with ceftriaxone resistant Enterobacterales bacteremia in order to advise local practices.

Methods: Ceftriaxone-resistant *E. coli*, *K. pneumoniae, K. oxytoca* and *P. mirabilis* were obtained from adult inpatient blood cultures between March 2016 and June 2020 and subsequently frozen. Isolates were regrown from frozen stock and ESBL status confirmed with phenotypic disc testing. For piperacillin/tazobactam-sensitive isolates, patient charts were reviewed for admission and antimicrobial treatment data including outcomes of death, bacteremia relapse, and hospital readmission.

Results: Of 84 ceftriaxone-resistant isolates, 62 were ESBL positive (73.8%). 60 were susceptible to piperacillin/tazobactam. Of 51 ESBL-producing isolates in this cohort, 23 patients received definitive BLBLI treatment (piperacillin/tazobactam or amoxicillin/clavulanate), and 28 definitive non-BLBLI treatment, primarily carbapenems. Preliminary 30-day outcomes suggest similar rates of death (13.0% vs. 10.7%), relapse (8.7% vs. 7.1%), and readmission (17.4% vs. 25.0%) amongst ESBL positive infections treated with BLBLI and non-BLBLI respectively.

Conclusions: Approximately 74% of ceftriaxone resistant Enterobacterales blood isolates were ESBL positive, suggesting ceftriaxone resistance to be a pragmatic proxy for ESBL positivity without need for phenotypic testing. Preliminary clinical outcomes were similar for BLBLI- and non-BLBLI-treated ESBL infections, but small numbers limit generalizability. Implementing modified BLBLI sensitivity reporting in ceftriaxone-resistant isolates in favour of carbapenems should only impact a relatively small number of patients, approximately 1-2 per month in our centre.